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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,188	02/16/2001	Mark Tuszynski	041673/2045	5329
30542	7590	03/10/2004	EXAMINER	
FOLEY & LARDNER P.O. BOX 80278 SAN DIEGO, CA 92138-0278			CHEN, SHIN LIN	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

18/4

Office Action Summary

Application No.

09/788,188

Applicant(s)

TUSZYNSKI ET AL.

Examiner

Shin-Lin Chen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-6 and 8-25 is/are pending in the application.
- 4a) Of the above claim(s) 11-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-6 and 8-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicants' amendment filed 1-8-04 has been entered. Claims 3 and 7 have been canceled. Claims 1 and 5 have been amended. Claims 1, 2, 4-6 and 8-25 are pending. Claims 1, 2, 4-6 and 8-10 are under consideration.

Applicants request reconsideration of restriction requirement and examination of SEQ ID Nos. 2, 4, 6 and 8 all together. Applicants argue that MPEP guideline allow up to 10 sequences to be examined together for a patent application. Applicants cite Ebendal, 1992, and argue that family of neurotrophin are substantially homologous and share substantially similar bioactivity (amendment, p. 5, 6). This is not found persuasive because of the reasons of record. SEQ ID Nos. 2, 4, 6 and 8 represent different and distinct DNA sequences derived from different genes. Although they have same N-glycosylation sequence and same kind of mutation in that sequence, they represent amino acid sequences of different genes having different biological functions. Sequence search of 10 sequences in a patent application imposes substantial burden on patent examination by examiner. Further, although Ebendal indicates NFG, BDNF, NT-3, and NT-4/5 are in the gene family of neurotrophin, Ebendal shows that there are 5 variable regions within NGF, NT-3, BDNF, and NT-4/NT-5. Although there are 6 cysteine residues common to all known neurotrophins, they have different amino acid sequences, e.g. 5 variable regions, and have different biological functions. NGF binds to trk tyrosine protein kinase receptor, BDNF and NT-3 bind to trkB protein, and NT-3 binds to trkC protein (e.g. Ebendal, p. 465). Trk, trkB, and trkC maybe in the same gene family, however, they are different receptor proteins, therefore, the neurotrophin proteins bind to different receptor proteins. In addition, "particular regions of NGF and BDNF result in the specific actions on different populations of responding neurons"

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(e.g. Ebendal, p. 467, left column), thus, NGF and BDNF have different target neuronal cell populations. Therefore, SEQ ID Nos. 2, 4, 6 and 8 represent different proteins having different biological functions, and they are patentably distinct from each other.

The requirement is still deemed proper and remains FINAL.

This application contains claims 11-25 drawn to an invention nonelected with traverse in Paper Nos. 13 and 16. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

The claim page (specification, page 15) should start with "I claim", "We claim", or "What is claimed is" but **not** "Claim". Appropriate correction is required. Applicants fail to respond to this objection.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 9 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention and is repeated for the reasons set forth in the preceding Official action mailed 9-8-

03. Applicant's arguments filed 1-8-04 have been fully considered but they are not persuasive.

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Applicants argue that claim 9 is in proper Markush group format and requires neither “comprising” or “consisting essentially of” language. This is not found persuasive because it is still unclear whether the mutant pro-neurotrophin precursor polypeptide “comprises” or “consists of” amino acid sequence of SEQ ID No. 2, 4, 6, or 8. The phrase “A mutant pro-neurotrophin precursor polypeptide selected from the group of polypeptides consisting of SEQ ID Nos. 2, 4, 6, and 8” does not specify the relationship between the mutant precursor polypeptide and the SEQ ID Nos.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-8 and 10 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and is repeated for the reasons set forth in the preceding Official action mailed 9-8-03. Applicant's arguments filed 1-8-04 have been fully considered but they are not persuasive.

Applicants argue that the “family of neurotrophins” as indicated in the specification page 1, lines 21 to 32, does not include “other nervous nervous system growth factors” as described on page 2 lines 1-10 of the specification (amendment, p. 8). This is not found persuasive because of

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the reasons set forth in the preceding Official action mailed 9-8-03. NGF includes alpha-NGF, beta-NGF and gamma-NGF. The claims encompass any mutant pro-neurotrophin of various NGF, BDNF, NT-3, and NT-4/5 derived from numerous different organisms, such as humans, mice, rats, bovines, ovines, birds, other mammals, fishes, and insects etc. The specification fails to provide sufficient description for the cleavage site of various NGF, BDNF, NT-3, and NT-4/5 proteins derived from numerous different organisms and whether either at a position 8 amino acids or 4 amino acids upstream of said cleavage site would be an asparagine that can be substituted with a basic residues, such as serine.

5. Claims 1-8 and 10 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the amino acid sequence comprising SEQ ID No. 2, does not reasonably provide enablement for any mutant pro-neurotrophin having an asparagine residue at a position 8 amino acids or at a position 4 amino acids upstream of the cleavage site for the mature growth factor substituted with a basic residue, such as serine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 9-8-03. Applicant's arguments filed 1-8-04 have been fully considered but they are not persuasive.

Applicants argue that the “family of neurotrophins” as indicated in the specification page 1, lines 21 to 32, does not include “other nervous nervous system growth factors” as described on page 2 lines 1-10 of the specification (amendment, p. 8). This is not found persuasive because of

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the reasons set forth in the preceding Official action mailed 9-8-03 and the reasons set forth above.

It should be noted that the subject matter of “An isolated mutant pro-neurotrophin precursor polypeptide comprising amino acid sequence of SEQ ID No. 2” in the present application is considered allowable.

Conclusion

No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.



**SHIN-LIN CHEN
PRIMARY EXAMINER**